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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,099	02/06/2007	Shuji Terashima	P29763	9412

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/575,099	TERASHIMA ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *19-29 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/29/2009 has been entered.

Claims 19-29 and 34 have been withdrawn.

Claims 1-18 and 30-33 are under examination.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 12-17 of U.S. Patent No. 6,268,119 in view of each Oka et al. (U.S. Patent No. 5,298,165, of record), Oka et al. (PGPUB 2004/0251195, of record), Fukuda et al. (WO 02/087660, Abstract, of record), and Rubinstein et al. (Proc. Natl. Acad. Sci. USA, 1995, 92: 10119-10112, of record).

The instant claims are drawn to a method of preparing a concentrate of nucleated cells by introducing a cell-containing solution which contains both nucleated cells and unnecessary cells into a filter device comprising an inlet and an outlet, wherein the filter device capture the nucleated cells and discharges the unnecessary cells, followed by the addition of a recovery solution to recover the nucleated cells captured by the filter; before being introduced into the filter device, the cell-containing solution is separated into a layer rich in nucleated cells, a nucleated cell-diluted layer (i.e., plasma), and a layer rich in unnecessary cells, wherein the layer rich in unnecessary cells is the first to be introduced into the filter device, followed by nucleated cell-diluted layer and the layer rich in nucleated cells in this order; the recovery solution could be the nucleated cell-diluted layer (i.e., plasma) and the recovery solution is further centrifuged to concentrate the nucleated cells (claims 1, 7-10, and 30-33). Separation of the cell-containing solution into layers takes place by centrifugation or by agglutination with hydroxyethyl starch (HES) followed by centrifugation (claims 2, 3, and 6), the unnecessary cells are erythrocytes, and the nucleated cells are hematopoietic

stem cells (claims 4 and 5). The filter device further contains an aggregate-capturing material between the inlet and the filter and a porous recovery solution-rectifying material between the filter and the outlet; the filter and the recovery solution-rectifying material form a porous filter material wherein the value obtained by dividing the effective filtration area of the filter material by the thickness of the nucleated cell-capturing filter is between 15 and 120 cm (claims 11-13). The filter material is non-woven fabric (having an average fiber diameter of 1.1-3.0 μm for the cell-capturing material or 0.5-1.5 μm for the rectifying material, with a packaging density of 0.1-0.3 g/cm^3), a sponge-like structure (having an average pore diameter of 7-25 μm for the cell-capturing material or of 2-10 μm for the rectifying material, with a porosity between 55 and 90%), or a combination of a non-woven fabric with a sponge-like structure (claims 14-18).

The patent claims recite a cell separation method comprising introducing a fluid containing cells to be recovered and cells to be removed into a cell-capturing device having an inlet and an outlet and a cell-capturing means which captures the cells to be recovered and discharges the cells to be removed, followed by the introduction of a liquid into the cell-capturing means to recover the captured cells; the cell-capturing means comprises non-woven fabrics with a fiber diameter of 1.0-30 μm or porous spongy structure having a pore size of 2.0-25 μm (claims 1, 6, and 12). The cells to be recovered are nucleated cells such as hematopoietic stem cells and the cells to be removed are erythrocytes (claims 13-17). The specification defines that the liquid used to recover the captured cells could be plasma (p. 8, lines 21-51, p. 12, line 63 through lines 1-5 of p. 13). The patent claims do not recite a composite filter comprising an

aggregate-capturing material, a nucleated cell-capturing material, and a recovery solution rectifying material, nor do they recite using centrifugation to separate the cell-containing solution into a layer rich in nucleated cells, a nucleated cell-diluted layer, and a layer rich in unnecessary cells before introducing it into the filter device or adding HES before centrifuging the cell-containing solution. However, at the time the invention was made, such limitations were well known and used in the prior art. For example, Oka et al. (U.S. Patent NO 5,298,165) teach improved leukocyte capturing by using a composite filter comprising a pre-filter (i.e., an aggregate-capturing material), a nucleated cell-capturing filter, and a microfilter, in this order (Abstract, column 8, lines 25-45, column 10, lines 19-30 and 62-67, column 11, lines 1-16). It is noted that the instant specification defines the recovery solution rectifying material as a porous filter having a packing density of 0.1-0.3 g/cm^3 and an average fiber diameter of 0.5-1.5 μm (p. 19, second full paragraph). Since Oka et al. (U.S. Patent NO 5,298,165) teach their microfilter as having a packing density of 0.15-0.38 g/cm^3 and a fiber diameter of 0.5-1.4 μm (column 8, lines 60-66, column 12, lines 53-55), their microfilter has the same properties as the claimed recovery solution rectifying material, i.e., their microfilter is a recovery solution rectifying material. In addition, both Oka et al. (PGPUB 2004/0251195) and Fukuda et al. teach a method for isolating nucleated cell from blood, the method comprising centrifuging the blood, i.e., separating the blood into a buffy coat (layer rich in nucleated cells), plasma (nucleated cell-diluted layer), and an erythrocyte pellet (layer rich in unnecessary cells), followed by introducing the separated blood into a filter device, wherein such a separation results in high retention of nucleated cells on

the filter (see Oka et al., p. 1, paragraphs 0005 and 0010; Fukuda et al., Abstract). Rubinstein et al. teach adding HES to blood to enhance erythrocyte sedimentation (p. 10120, column 2, third paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the patent claims by introducing the HES/centrifugation steps and using a composite filter as taught by the prior art, with a reasonable expectation of success. One of skill in the art would have been motivated to do so because the art teaches that such modifications result in increased retention of nucleated cells within the filter device. With respect to the different values recited in the instant claims 11, 12, 15, and 17, it would have been obvious to one of skill in the art to vary the parameters (i.e., fiber or pore size and packaging density) to optimize the results according to the nucleated cell to be separated. With respect to centrifuging the recovery solution, it would have been obvious to one of skill in the art to do such in order to further concentrate the recovered nucleated cells. With respect to using a combination between a non-woven and a sponge-like material, it would have been obvious to one of skill in the art to do so in order to improve the performance of the filter device. With respect to the limitation of the recovery solution being nucleated cell diluted layer (i.e., plasma, see above), since the specification defines that the recovery solution could plasma, it would have been obvious to one of skill in the art to use such a layer to achieve the predictable result of recovering the nucleated cells. Thus, the instant claims and patent claims are obvious variants.

The applicant refers the Office to the prior arguments made in the prior response, all of which are maintained. In addition, the applicant argues that the rejection is improper. The applicant submits that an obviousness-type double patenting rejection is intended to prevent the applicants (i.e., the assignee or a common inventor) from improperly extending the right to exclude under an earlier patent. Applicants note that MPEP 804 sets forth the policy behind obvious-type double patenting rejections:

> The doctrine of double patenting seeks to prevent the unjustified extension of patent exclusivity beyond the term of a patent. The public policy behind this doctrine is that: The public should.., be able to act on the assumption that upon the expiration of the patent it will be free to use not only the invention claimed in the patent but also modifications or variants which would have been obvious to those of ordinary skill in the art at the time the invention was made, taking into account the skill in the art and prior art other than the invention claimed in the issued patent. In re Zickendraht, 319 F.2d 225, 232, 138 USPQ 22, 27 (CCPA 1963) (Rich, J., concurring). Double patenting results when the right to exclude granted by a first patent is unjustly extended by the grant of a later issued patent or patents. In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982).

As very clearly stated above, the issue is one of extension of rights in claims. That is, the policy seeks to prevent an unwarranted extension of patent rights. This is most often seen in a genus-species relationship, where an earlier genus claim is the basis for an obviousness-type double patenting rejection of a later species claim, or vice versa. There are other examples in which an obviousness-type double patenting rejection can properly be raised, but in every instance, there is an underlying public policy concern that rights in an earlier patent would be unfairly extended by the later application's claims. Because the focus of an obviousness-type double patenting rejection is an unjust extension of the rights to exclude, the question is whether the later claims would be obvious in view of the earlier claims. As noted in MPEP 804,

> When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. General Foods Corp. v. Studiengesellschaft Kohle mbH, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure.
> The specification can be used as a dictionary to learn the meaning of a term in the patent claim. Toro Co. v. White Consol. Indus., Inc., 199 F.3d 1295, 1299, 53 USPQ2d 1065, 1067 (Fed. Cir. 1999)C[W]ords in patent claims are given their ordinary meaning in the usage of the field of the invention, unless the text of the patent makes clear that a word was used with a special meaning."); Renishaw PLC v. Marposs Societa"per Azioni, 158 F.3d 1243, 1250, 48 USPQ2d 1117, 1122 (Fed. Cir. 1998) ("Where there are several common meanings for a claim term, the patent disclosure serves to point away from the improper meanings and toward the proper meanings."). See also MPEP § 2111.01. Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970).

The applicant argues that obviousness *per se*, which prevents a patent applicant from obtaining a patent claim to an invention that would be obvious in view of the prior art, is addressed separately under 35 U.S.C. § 103. While the MPEP explains that the analysis is similar, the two prohibitions are separate, and they separately prevent different activities. Obviousness-type double patenting rejections seek to prevent the granting of claims that are obvious in view of prior claims, whereas 35 U.S.C. § 103 seeks to prevent the granting of claims that are obvious in view of prior disclosure. If an obviousness-type double patenting rejection could be made simply by combining the claims in one prior art patent with the disclosure of another patent, the distinction between the two prohibitions would be meaningless, and an obviousness-type double patenting rejection would be available to the Patent Office in practically every instance in which an applicant's own prior art was the basis for a prior art rejection.
The applicant submits that this is exactly what the Office has done in this instance: take a prior art rejection under 35 U.S.C. § 103 and simply reuse it in an obviousness-type

double patenting rejection. The applicant argues that such practice by the Office is not supported by the MPEP, the Rules, Statutes, or any relevant case law.

The applicants requests that, if the Examiner chooses to maintain this rejection, that she specifically explain how the instant claims constitute an unjust extension of the claims of SUMITA. That is, focusing on the public policy "that upon the expiration of the patent [the public] will be free to use not only the invention claimed in the patent but also modifications or variants which would have been obvious to those of ordinary skill in the art at the time the invention was made, taking into account the skill in the art and prior art other than the invention claimed in the issued patent".

The applicant's arguments are acknowledged; however, they are not found persuasive for the following reasons:

Most of the applicant's arguments are not new, were previously addressed in the final Office action of 07/01/2009 and not found persuasive. The additional arguments are practically the same as the arguments. Basically, the applicant argues again that it is improper to make an obviousness-type double patenting rejection in view of prior art. This argument was not found persuasive for the reasons of record set froth in the final Office action of 07/01/2009. Even the citation from MPEP 804 provided by the applicant stating that, upon the expiration of the patent, the public "will be free to use not only the invention claimed in the patent but also modifications or variants which would have been obvious to those of ordinary skill in the art at the time the invention was made, taking into account the skill in the art and prior art other than the invention claimed in the

issued patent" provides for the use of prior art references when making obviousness-type double patenting rejections (see also MPEP 804, formed paragraphs 8.36 and 8.37). Therefore, MPEP provides the basis to make the instant obviousness-type rejection over the claims of the U.S. Patent No. 6,268,119 in view of the disclosure in the prior art. It is noted that the applicant did not provide any evidence indicating that it would not have been obvious to one of skill in the art to arrive at the claimed invention by modifying the claims of the U.S. Patent No. 6,268,119 according to the cited prior art.

Moreover, because the U.S. Patent No. 6,268,119 patent qualifies as prior art, it is also proper to use it to reject the instant claims under 103(a) (see MPEP 804).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-17 and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sumita et al. (U.S. Patent No. 6,268,119, of record), in view of each Oka et al. (U.S. Patent No. 5,298,165, of record), Fukuda et al. (WO 02/087660, of record), Oka et al. (PGPUB 2004/0251195, of record), and Rubinstein et al. (Proc. Natl. Acad. Sci. USA, 1995, 92: 10119-10122, of record).

Sumita et al. teach a method of preparing a nucleated cell concentrate by introducing blood into a filter device comprising a filter material capable of capturing nucleated cells and discharging unnecessary cells, followed by the introduction of a recovery solution to elute the captured nucleated cells; the filter material could be a non-woven fabric with a diameter of 1-30 μm or a spongy structure with a pore size of 3-20 μm, the nucleated cells are hematopoietic stem cells, the unnecessary cells are erythrocytes, and the recovery solution could be plasma (claims 1, 4, 5, 30, 32, and 33) (column 2, lines 51-67, column 3, lines 1-8 and 50-55, column 5, lines 18-67, column 6, lines 27-60, column 8, lines 21-51, p. 12, line 63 through lines 1-5 of p. 13).

Sumita et al. do not teach a composite porous filter material comprising, in a direction from the inlet to the outlet, an aggregate-capturing material, a nucleated cell-capturing material, and a recovery solution-rectifying material, wherein the filter material comprises a non-woven fabric, a sponge-like structure, or a combination between a non-woven fabric and a sponge-like structure (claims 11-17). Oka et al. (U.S. Patent NO 5,298,165) teach improved leukocyte capturing by using a porous composite filter made of a non-woven material comprising in the upstream to downstream order: a pre-filter (i.e., an aggregate-capturing material), a nucleated cell-capturing filter, and a microfilter (Abstract, column 8, lines 25-45, column 10, lines 19-30 and 62-67, column 11, lines 1-16). The porous composite filter of Oka et al. (U.S. Patent NO 5,298,165) has an average fiber diameter of 1.0-2.0 μm for the nucleated cell-capturing material and of 0.5-1.4 μm for the microfilter material and a packing density of 0.15-0.38 g/cm^3 (claim 15) (column 8, lines 60-66, column 10, lines 19-30). With respect to the limitation

of recovery solution rectifying material, it is noted that the instant specification defines the recovery solution rectifying material as a porous filter having a packing density of 0.1-0.3 g/cm^3 and an average fiber diameter of 0.5-1.5 μm (p. 19, second full paragraph). Since Oka et al. (U.S. Patent NO 5,298,165) teach their microfilter as having a packing density of 0.15-0.38 g/cm^3 and a fiber diameter of 0.5-1.4 μm (column 8, lines 60-66, column 12, lines 53-55), their microfilter has the same properties as the claimed recovery solution rectifying material, i.e., their microfilter is a recovery solution rectifying material. Therefore, Oka et al. (U.S. Patent NO 5,298,165) teach a porous composite filter comprising in a direction from the inlet to the outlet, an aggregate-capturing material, a nucleated cell-capturing material, and a recovery solution-rectifying material. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the filter device of Sumita et al., by using the composite filter device of Oka et al. (U.S. Patent NO 5,298,165), with a reasonable expectation of success. The motivation to do so is provided by Oka et al. (U.S. Patent NO 5,298,165), who teach that composite filters are very efficient in removing nucleated cells from blood. One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that composite filters can be successfully used to capture blood nucleated cells. With respect to the limitations recited in claim 17, Oka et al. (U.S. Patent NO 5,298,165) teach an average pore diameter of 6-20 μm for the nucleated cell-capturing material, of 4-12 μm for the recovery solution-rectifying material and a packing density of 0.15-0.38 g/cm^3 (column 10, lines 41-45, column 12, lines 53-55). Therefore, it would have been obvious to one

of skill in the art, at the time the invention was made, to modify the sponge-like filter of Sumita et al. according to the teachings of Oka et al. (U.S. Patent NO 5,298,165) to achieve the predictable result of obtaining a composite sponge-like filter with improved properties.

Sumita et al. and Oka et al. (U.S. Patent NO 5,298,165) do not teach using centrifugation to separate the cell-containing solution into a layer rich in nucleated cells, a nucleated cell-diluted layer, and a layer rich in unnecessary cells before introducing it into the filter device or adding HES before centrifuging the cell-containing solution (claims 1-3 and 6-8). However, at the time the invention was made, such limitations were well known and used in the prior art. For example, both Oka et al. (PGPUB 2004/0251195) and Fukuda et al. teach a method for isolating nucleated cell from blood, the method comprising centrifuging the blood with the simultaneous introduction of the separated components into nucleated cell-capturing filters, wherein the method results in high retention of nucleated cells on the filter (see Oka et al., p. 1, paragraphs 0005 and 0010, p. 2, paragraph 0017; Fukuda et al., Abstract). Such a method would necessarily result in a cell gradient comprising a buffy coat at the top (layer rich in nucleated cells), plasma in the middle (nucleated cell-diluted layer), and an erythrocyte pellet at the bottom (layer rich in unnecessary cells) with the introduction into the filter of the separated components in the order of erythrocyte pellet first, plasma second, and buffy coat third (claims 1, 7, and 8). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Sumita et al. and Oka et al. (U.S. Patent NO 5,298,165) by introducing into the filter device a blood cell gradient as

taught by Fukuda et al. and Oka et al. (PGPUB 2004/0251195), with a reasonable expectation of success. The motivation to do so is provided by Fukuda et al., who teach that such a method results in high retention of nucleated cells on the filter (Abstract). One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that such steps can be successfully used to obtain nucleated cells from blood. Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., and Oka et al. (PGPUB 2004/0251195) do not teach using HES in combination with centrifugation (claims 3 and 6). Rubinstein et al. teach adding HES to blood to enhance erythrocyte sedimentation (p. 10120, column 2, third paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., and Oka et al. (PGPUB 2004/0251195) by introducing the HES before the centrifugation step, with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to improve separation of blood into its components. One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that HES improves erythrocyte elimination. With respect to the limitation of the filter having value obtained by dividing the effective filtration area by the thickness of the nucleated cell-capturing material of 15-120 cm (claims 11 and 12) or of porosity of 55-90% (claim 17), it would have been obvious to one of skill in the art to use routine experimentation to vary these parameters to optimize the results according to the nucleated cell to be separated (see Oka et al., U.S. Patent NO 5,298,165, column 6, lines 3-9). With

respect to centrifuging the recovery solution (claim 10), it would have been obvious to one of skill in the art to do such in order to further concentrate the recovered nucleated cells. With respect to the limitation of the recovery solution being nucleated cell diluted layer (claim 9), since Sumita et al. teach that plasma can be used s a recovery solution and since the nucleated cell diluted layer is plasma (see above), it would have been obvious to one of skill in the art to use such a layer to achieve the predictable result of recovering the nucleated cells.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

6. Claims 1-18 and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sumita et al. taken with each Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al., in further view of Tanaka et al. (U.S. Patent No. 6,048,464).

The teachings of Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al. are applied as above for claims 1-17 and 30-33. Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al. do not teach a filter made from a combination of non-woven fabric with a sponge-like structure (claim 18). However, at the time the invention was made, such combination filters were taught by the prior art. For example, Tanaka et al. teach a nucleated cell-capturing filter comprising both a sponge-like structure and a non-woven fabric (Abstract, column 3,

lines 19-46, column 6, lines 17-26). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al. by using a combination filter comprising both a sponge-like structure and a non-woven fabric to achieve the predictable result of capturing nucleated cells.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

The applicant notes that the present invention recites, "the layer rich in unnecessary cells is first introduced into the above-described filter device, and the layer rich in nucleated cells is then introduced therein, so as to discharge the unnecessary cells remaining in the above-described filter device while capturing the nucleated cells by the above-described filter material, and a recovery solution is then introduced into the above-described filter device." According to the Office Action, OKA 2 and FUKUDA teach the introduction of a layer rich in unnecessary cells first (pellet), then the recovery solution (plasma), then the layer rich in nucleated cells (buffy coat). The applicant argues that this order reverses the order of the last two elements in the instant claims, and thus, does not teach or suggest these elements. The applicant notes that this point is particularly true with respect to claim 9, as the Office Action specifically states that SUMITA teaches that plasma can be used as the recovery solution. (Office Action, page 12, lines 8-12.) However, if it is the Office's position that the plasma of OKA 2 and FUKUDA is not the recovery solution, and that some additional recovery solution would

be used, the applicant request that the Office point to such disclosure, or explain why such additional step would be obvious. Still further, in the event that the Office believes that an additional recovery solution would be used, the applicant requests that the Office explain how claim 9 would be obvious - as the two positions would appear to be inconsistent. Even assuming *arguendo* that the cited documents teach the order of introduction of unnecessary cells first, nucleated cells second, and plasma third, one of skill in the art would not have turned to OKA 2 or FUKUDA at least because FUKUDA teaches blood fractions containing 1) erythrocytes, granulocytes, and monocytes, 2) lymphocytes, and 3) platelets and plasma (page 4, [0063]). Furthermore, OKA 2 teaches the removal of white blood cells, not their collection.

The applicant's arguments are acknowledged; however, they are not found persuasive for the following reasons:

The instant claims are drawn to a method of preparing a nucleated cell concentrate by first separating a cell-containing solution into a layer rich in nucleated cells, a nucleated cell-diluted layer, and a layer rich in unnecessary cells and introducing these layers into a filter such that the layer rich in unnecessary cells is introduced first, followed by the nucleated cell-diluted layer and then by the layer rich in nucleated cells (see the instant claims 1 and 7). As noted in the rejection above, OKA 2 and FUKUDA teach the introduction of a layer rich in unnecessary cells first, then the plasma (which is the nucleated cell-diluted layer), then the layer rich in nucleated cells, i.e., the order recited in claims 1 and 7. That the nucleated cell-diluted layer can also be

used as a recovery solution does not change this. The rest of the applicant's arguments are not material to the instant rejection because the instant rejection clearly states that plasma, and not "some additional solution", is used as the recovery solution.

The applicant argues that one of skill in the art would not have turned to OKA 2 or FUKUDA. This is just an argument not supported by any evidence and therefore, it is not found persuasive.

Conclusion

7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633